L Number	Hits	Search Text	DB	Time stamp
1	42	hbv same "131"	USPAT; US-PGPUB; DERWENT	2003/06/19 08:34
2	0	"solution phase primer is labelled with a reporter molecule"	USPAT; US-PGPUB; DERWENT	2003/06/19 08:36
3	4	hbv and capturable	USPAT; US-PGPUB; DERWENT	2003/06/19 08:36
4	1	(hbv and capturable) and library	USPAT; US-PGPUB; DERWENT	2003/06/19 08:37
5	3	(hbv and capturable) and red	USPAT; US-PGPUB; DERWENT	2003/06/19 08:37
6	0	(hbv and capturable) and orcein	USPAT; US-PGPUB; DERWENT	2003/06/19 08:38
7	1	orcein near red	USPAT; US-PGPUB; DERWENT	2003/06/19 08:39
8	3	(hbv and capturable) and lamivudine	USPAT; US-PGPUB; DERWENT	2003/06/19 08:39

(FILE 'HOME' ENTERED AT 07:32:07 ON 19 JUN 2003)

FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, SCISEARCH' ENTERED AT 07:32:24 ON 19 JUN 2003

L1 68029 S HEPATITIS B VIRUS SURFACE ANTIGEN OR HBSAG OR HBV
L2 121680 S 131 OR T131N OR T131 OR N131 OR ('T 131 N')
L3 270 S L1 AND L2
L4 100 DUP REM L3 (170 DUPLICATES REMOVED)
L5 16 S L4 AND (MUTANT? OR MUTATION? OR VARIANT? OR ALLELE?)

=>

L5 ANSWER 1 OF 16 MEDLINE
ACCESSION NUMBER: 2001136629 MEDLINE
DOCUMENT NUMBER: 20540797 PubMed ID: 11092260
TITLE: De novo acute hepatitis B infection in a previously vaccinated liver transplant recipient due to a strain of **HBV** with a Met 133 Thr **mutation** in the "a" determinant.
AUTHOR: Yoshida E M; Ramji A; Erb S R; Davis J E; Steinbrecher U P; Sherlock C H; Scudamore C H; Chung S W; Williams M; Gutfreund K S
CORPORATE SOURCE: British Columbia Transplant Society and the Department of Medicine, University of British Columbia, Vancouver, Canada.
SOURCE: LIVER, (2000 Oct) 20 (5) 411-4.
Journal code: 8200939. ISSN: 0106-9543.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200103
ENTRY DATE: Entered STN: 20010404
Last Updated on STN: 20010404
Entered Medline: 20010301

AB De novo **HBV** infection post-liver transplantation (LT) from an anti-HBc seropositive donor rarely presents as acute failure. We report a 42-year-old Caucasian female, **HBsAg** and anti-HBc seronegative, with primary biliary cirrhosis who received an allograft from a **HBsAg** negative, anti-HBc seropositive donor. The patient, previously vaccinated years pre-LT, was re-vaccinated against **HBV** and 1 year post-LT had an anti-HBs titre of 256 IU/l. Two years post-LT, elevated serum aminotransferases and worsening liver function with an INR of 2.0 developed. The **HBsAg** became positive, anti-HBs undetectable and serum **HBV**-DNA >2000 pg/ml by hybridisation assay. Liver biopsy revealed significant ballooning degeneration, piecemeal necrosis and positive immunostaining for **HBsAg**. Progressive liver failure developed followed by sepsis and terminal multi-organ failure. Subsequent analysis of the predominant **HBV** strain revealed **mutations** in the "a" determinant: Met 133 Thr (codon change ATG to ACG) and Asn **131** Thr. CONCLUSION:' Acute de novo **HBV** infection from an anti-HBc sero-positive donor may occur long after LT despite protective anti-HBs titres post-vaccination secondary to the emergence of "a" determinant mutated strains of **HBV**.

L5 ANSWER 2 OF 16 MEDLINE
ACCESSION NUMBER: 2000394824 MEDLINE
DOCUMENT NUMBER: 20376462 PubMed ID: 10921048
TITLE: Universal presence of HBVx gene and its close association with hotspot **mutation** of p53 gene in hepatocellular carcinoma of prevalent area in China.
AUTHOR: Zhang F; Zhu Y; Sun Z
CORPORATE SOURCE: Cancer Institute, Chinese Academy of Medical Sciences, Peking Union Medical College, Beijing.
SOURCE: CHUNG-HUA CHUNG LIU TSA CHIH [CHINESE JOURNAL OF ONCOLOGY], (1998 Jan) 20 (1) 18-21.
Journal code: 7910681. ISSN: 0253-3766.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200008
ENTRY DATE: Entered STN: 20000824
Last Updated on STN: 20000824

Entered Medline: 20000811

AB OBJECTIVE: Hepatitis B virus (**HBV**) is a major etiological agent of hepatocellular carcinoma (HCC). The x gene of **HBV** genome (HBVx) is considered as its oncogene. In order to assess the extent of its involvement in hepatocarcinogenesis, both **HBsAg** sero-positive and mainly sero-negative HCC were searched for the presence, expression and **mutation** status of the x gene of **HBV**, as well as its association with 249 codon hot spot **mutation** of p53 gene. METHODS: Using PCR, RT-PCR, PCR-RFLP and DNA sequencing, studies were more focused on 25 **HBsAg** sero-negative, pathologically diagnosed HCC patients operated during 1991 to 1996 mainly in Qidong and also in Beijing. RESULTS: The x gene sequence of **HBV** was found by PCR without exception in all 25 seronegative HCC DNA (100% 25/25) and also in all 19 seropositive counterparts. The RNA messages of HBVx gene were found in all 8 HCC patients randomly selected from the seronegative group. Sequence analysis of the HBVx gene showed the presence of missense **mutation** in the 130 and **131** codon in 4 of 6 samples studied. Using PCR-RFLP, missense **mutation** of the 249 codon was identified in 57% (12/21) of all **HBsAg** negative cases from Qidong. No such **mutations** were found in the 4 Beijing counterparts. CONCLUSION: HBVx gene sequence was universally present in **HBsAg** negative HCC samples of Qidog studied, indicating the important role of HBVx gene in hepatocarcinogenesis of the high incidence area. The close association of the hotspot **mutation** of p53 gene in Qidong HCC with the presence of HBVx gene sequence suggests that such **mutation** is the molecular footprint of the combined effect of aflatoxin B1 exposure and HBVx gene product.

L5 ANSWER 3 OF 16 MEDLINE
ACCESSION NUMBER: 2000211737 MEDLINE
DOCUMENT NUMBER: 20211737 PubMed ID: 10745226
TITLE: Unusual hepatitis B surface antigen variation in a child immunised against hepatitis B.
AUTHOR: Roznovsky L; Harrison T J; Fang Z L; Ling R; Lochman I; Orsagova I; Pliskova L
CORPORATE SOURCE: Department of Infectious Diseases, University Hospital, Ostrava, Czech Republic.. ludek.roznovsky@fnspo.cz
SOURCE: JOURNAL OF MEDICAL VIROLOGY, (2000 May) 61 (1) 11-4. Journal code: 7705876. ISSN: 0146-6615.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200007
ENTRY DATE: Entered STN: 20000810
Last Updated on STN: 20000810
Entered Medline: 20000724

AB Perinatal transmission of and infection with hepatitis B (**HBV**) in early childhood are observed in a small proportion of the offspring of hepatitis B surface antigen (**HBsAg**)-positive mothers who are vaccinated against **HBV** immediately after giving birth. The children may be infected by wild-type **HBV** or by **variants** with amino acid substitutions in the "a" determinant of **HBsAg**, particularly at position 145 and, rarely, at positions 120, 126, 129, **131**, 141, and 144. Four hundred and forty-six newborn infants of **HBsAg**-positive mothers in the northeastern part of the Czech Republic received combined active and passive immunisation against **HBV**. Only one child became an **HBsAg** carrier. This followed a mild, acute **HBV** illness in the beginning of the second year of his life. **HBV** DNA encoding the "a" determinant and surrounding region of **HBsAg** was sequenced after amplification from the plasma of the child and his mother. The child was infected with **variants** of **HBsAg** with substitutions at

residues 137 and 139. The virus of the mother had changes at residues 120 and 121. **HBV** from both child and mother had an unusual substitution at residue 118 and seemed to be of the ayw subdeterminant. Copyright 2000 Wiley-Liss, Inc.

L5 ANSWER 4 OF 16 MEDLINE
ACCESSION NUMBER: 2000180677 MEDLINE
DOCUMENT NUMBER: 20180677 PubMed ID: 10715787
TITLE: **HBV** transmission from father to foetus and **HBV** DNA in tissues outside the liver.
AUTHOR: Wang S; Jiang P; Peng G
CORPORATE SOURCE: Institute of Military Medicine, Guangzhou Command PLA.
SOURCE: CHUNG-HUA KAN TSANG PING TSA CHIH, (1999 Dec) 7 (4) 203-6.
Journal code: 9710009. ISSN: 1007-3418.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200003
ENTRY DATE: Entered STN: 20000330
Last Updated on STN: 20000330
Entered Medline: 20000323
AB OBJECTIVE: To study the possibility of **HBV** Transmission from father to foetus and **HBV** DNA in tissues outside liver. METHODS: Paired sera were from 8 **HBV** man carriers whose wives were negative for HBVM and 8 foetuses who were infected with **HBV** in the womb. S gene nt 451-660 nucleotide, C gene nt 2,022-2,321 nucleotide were directly sequenced. RESULTS: The homology of **HBV** sequence between father and foetus was very high. The **mutations** of 491, 494, 530, 546 and 581 nucleotide in the S gene caused 113, 114, 126, **131** and 143 amino acid substitution. **HBV** DNA can be detected in the tissues outside liver of foetus. CONCLUSION: **HBV** transmission from father to foetus may be present. **HBV** DNA in tissues outside liver of foetus can be detected.

L5 ANSWER 5 OF 16 MEDLINE
ACCESSION NUMBER: 2000147076 MEDLINE
DOCUMENT NUMBER: 20147076 PubMed ID: 10682495
TITLE: Detection of S-gene **mutation** strain in vertical transmission of **HBV** and its significance.
AUTHOR: Wang S; Jiang P; Peng G
CORPORATE SOURCE: Institute for Military Medicine, Guangzhou.
SOURCE: CHUNG-HUA LIU HSING PING HSUEH TSA CHIH CHINESE JOURNAL OF EPIDEMIOLOGY, (1999 Aug) 20 (4) 204-7.
Journal code: 8208604. ISSN: 0254-6450.
PUB. COUNTRY: China
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Chinese
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200004
ENTRY DATE: Entered STN: 20000505
Last Updated on STN: 20000505
Entered Medline: 20000425
AB OBJECTIVE: To study S-gene **mutation** of hepatitis B virus (**HBV**) in its vertical transmission and its significance. METHODS: Nucleotides of S-gene NT451-660 of **HBV** were sequenced with dideoxy end termination technique in four female and six male carriers without **HBV** markers in their spouses and in their intrauterine infected fetuses. RESULTS: It was showed that homology of **HBV** nucleotide and amino acid sequences in the mothers, fathers and their fetuses was very high. **Mutation** at the sites 491, 494, 530, 546 and 581 of S-gene resulted in amino acid substitution at the sites 113, 114, 126, **131** and 143, respectively. **Mutations** at the sites 126 were detected in two pairs of mother or father and her or his

fetuses and **mutations** at the sites **131** in four fetuses, respectively, including combined **mutation** at the site 143 in two fetuses. CONCLUSION: Strains with S-gene **mutation**, mainly at the sites 126, **131** and 143, could be found in **HBV** vertical transmissions, which could cause failure in HB vaccine immunization.

L5 ANSWER 6 OF 16 MEDLINE
ACCESSION NUMBER: 1999099013 MEDLINE
DOCUMENT NUMBER: 99099013 PubMed ID: 9882327
TITLE: Mechanism of suppression of hepatitis B virus precore RNA transcription by a frequent double **mutation**.
AUTHOR: Li J; Buckwold V E; Hon M W; Ou J H
CORPORATE SOURCE: Department of Molecular Microbiology and Immunology, University of Southern California School of Medicine, Los Angeles, California, USA.
SOURCE: JOURNAL OF VIROLOGY, (1999 Feb) 73 (2) 1239-44. Journal code: 0113724. ISSN: 0022-538X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199902
ENTRY DATE: Entered STN: 19990301
Last Updated on STN: 19990301
Entered Medline: 19990218

AB A double **mutation** which converts nucleotide 1765 from A to T and nucleotide 1767 from G to A is frequently found in the hepatitis B virus (**HBV**) genome isolated from **HBV** patients with chronic hepatitis symptoms. This double **mutation** is located in the core promoter that controls the transcription of the precore RNA and the core RNA. In addition, this double **mutation** also resides in the X protein coding sequence, converting codon 130 from Lys to Met and codon **131** from Val to Ile. Previous studies indicate that this double **mutation** removes a nuclear receptor binding site in the core promoter, suppresses specifically precore RNA transcription, and enhances viral replication. In this study, we further investigated how this double **mutation** suppresses precore RNA transcription. We found that this double **mutation** not only removed the nuclear receptor binding site but also created an HNF1 transcription factor binding site. Further transfection studies using Huh7 hepatoma cells indicate that the removal of the nuclear receptor binding site has no effect on the transcription of **HBV** RNAs, the two-codon change in the X protein sequence suppresses the transcription of both precore and core RNAs, and the creation of the HNF1 binding site restores the core RNA level. Hence, the specific suppression of precore RNA transcription by this frequent double-nucleotide **mutation** is the combined result of multiple factors.

L5 ANSWER 7 OF 16 MEDLINE
ACCESSION NUMBER: 1998114166 MEDLINE
DOCUMENT NUMBER: 98114166 PubMed ID: 9453421
TITLE: Detection of different viral strains of hepatitis B virus in chronically infected children after seroconversion from **HBsAg** to anti-HBs indicating viral persistence.
AUTHOR: Bahn A; Gerner P; Martine U; Bortolotti F; Wirth S
CORPORATE SOURCE: Children's Hospital of the Johannes Gutenberg University, Mainz, Germany.
SOURCE: JOURNAL OF HEPATOLOGY, (1997 Dec) 27 (6) 973-8. Journal code: 8503886. ISSN: 0168-8278.
PUB. COUNTRY: Denmark
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980226
Last Updated on STN: 19980226
Entered Medline: 19980219

AB BACKGROUND/AIMS: Seroconversion to anti-HBs or the loss of **HBsAg** is usually associated with complete elimination of the replicative hepatitis B virus. Usually in these patients hepatitis B virus DNA (**HBV** DNA) becomes undetectable. Routine controls of patients who underwent anti-HBs seroconversion by more sensitive tests showed that in some cases the virus persisted in the patient. Therefore the aim of our study was to evaluate if virus persistence could also be found in children with chronic hepatitis B after anti-HBs seroconversion. The virus pool should be characterized before and after seroconversion. METHODS: Viral DNA was extracted from nine **HBsAg** negative or anti-HBs positive sera of children, previously diagnosed as chronic **HBsAg** carriers. **HBV** DNA was amplified by polymerase chain reaction. Subsequently the nucleotide sequences of the polymerase chain reaction product in the a-determinant region (aa 121-161) were analyzed on an automatic fluorescent sequencer. RESULTS: In the sera of seven children, **HBV** DNA was detected in the **HBsAg** negative phase of the **HBV** infection. **Mutations** in codons 122, 125, 127, **131**, 134, 143, 159 and 161 of the S gene could be documented, resulting in amino acid changes. In three patients the sequence analysis revealed changes in the **HBV** genotype from genotype A (serotype adw) to genotype D (serotype ayw) during seroconversion to anti-HBs. CONCLUSIONS: These data demonstrate that persistence of the hepatitis B virus can also occur in **HBsAg** negative and anti-HBs positive children. After loss of **HBsAg**, no specific **HBV** **variant** was identified. Although a conclusive explanation for the selection process cannot be provided, it remains a fact that the 'surviving' viral strain was mostly represented by genotype D.

L5 ANSWER 8 OF 16 MEDLINE
ACCESSION NUMBER: 1998096389 MEDLINE
DOCUMENT NUMBER: 98096389 PubMed ID: 9434776
TITLE: Deletion **mutants** of the hepatitis B virus X gene in human hepatocellular carcinoma.
COMMENT: Erratum in: Biochem Biophys Res Commun 1998 Feb 13;243(2):640
AUTHOR: Hsia C C; Nakashima Y; Tabor E
CORPORATE SOURCE: Division of Transfusion Transmitted Diseases, Food and Drug Administration, Bethesda, Maryland, USA.
SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (1997 Dec 29) 241 (3) 726-9.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199802
ENTRY DATE: Entered STN: 19980217
Last Updated on STN: 19990129
Entered Medline: 19980203

AB Two patients with hepatocellular carcinoma (HCC) were identified who had substantial deletions within the hepatitis B virus (**HBV**) X gene from HCC tissues. In one patient, the deletion was found at nt. 382-389 (codons 128-130) of the X gene, followed by two nucleotide substitutions, a frame shift, and formation of a new stop codon. In the second patients, the deletion was found at nt. 389-396 (codons 130-132) of the X gene, followed by one nucleotide substitution, a frame shift, and formation of a new stop codon. The resulting X proteins in both cases would be truncated at the 3' end and would be 20 amino acids shorter than the full length X protein. These patients had been identified during a study of 25 HCC patients from Qidong, China in whom a 228-base region of the X gene was

sequenced. No deletions were found within this X gene sequence in HCC tissues from the other 23 patients or in the 20 adjacent noncancerous liver samples available from these patients. However, the fact that these deletions encompassed codons 130 and **131**, two adjacent codons where point **mutations** were found in 21 of the remaining 23 patients, suggests that this region may play an important role in hepatocarcinogenesis.

L5 ANSWER 9 OF 16 MEDLINE
ACCESSION NUMBER: 1998010925 MEDLINE
DOCUMENT NUMBER: 98010925 PubMed ID: 9349995
TITLE: Acute exacerbation of hepatitis due to reactivation of hepatitis B virus with **mutations** in the core region after chemotherapy for malignant lymphoma.
AUTHOR: Sato T; Kato J; Kawanishi J; Kogawa K; Ohya M; Sakamaki S; Niitsu Y
CORPORATE SOURCE: Fourth Department of Internal Medicine, Sapporo Medical University School of Medicine, Japan.
SOURCE: JOURNAL OF GASTROENTEROLOGY, (1997 Oct) 32 (5) 668-71. Journal code: 9430794. ISSN: 0944-1174.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199711
ENTRY DATE: Entered STN: 19971224
Last Updated on STN: 19971224
Entered Medline: 19971125
AB A 43-year-old Japanese man who was positive for hepatitis B surface (HBs) antigen and HB e antibody, underwent chemotherapy for non-Hodgkin's lymphoma. After the chemotherapy he suffered from acute exacerbation of hepatitis because of reactivation of **HBV**. Recovery was achieved with interferon-alpha, glucagon-insulin therapy, and plasma exchange. **Mutations** were detected in codons 97, 100, 129, and **131** of the core region of **HBV**. The peptide encoded from the core region including such **mutations** possibly had greater antigenicity to induce cytotoxic T cell activity in the host. Core region **mutations** may be a crucial cause of the acute exacerbation of hepatitis B seen after chemotherapy.

L5 ANSWER 10 OF 16 MEDLINE
ACCESSION NUMBER: 95154763 MEDLINE
DOCUMENT NUMBER: 95154763 PubMed ID: 7851832
TITLE: **Mutations** in the transcriptional regulatory region of the precore and core/pregenome of a hepatitis B virus with defective HBeAg production.
AUTHOR: Moriyama K; Takada T; Tsutsumi Y; Fukada K; Ishibashi H; Niho Y; Maeda Y
CORPORATE SOURCE: First Department of Internal Medicine, Faculty of Medicine, Kyushu University, Fukuoka, Japan.
SOURCE: FUKUOKA IGAKU ZASSHI. FUKUOKA ACTA MEDICA, (1994 Nov) 85 (11) 314-22. Journal code: 9423321. ISSN: 0016-254X.
PUB. COUNTRY: Japan
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: GENBANK-S75184
ENTRY MONTH: 199503
ENTRY DATE: Entered STN: 19950322
Last Updated on STN: 19960129
Entered Medline: 19950314
AB Termination **mutations** in the precore open reading frame of hepatitis B virus (**HBV**) **variants** with defective

hepatitis B e antigen (HBeAg) production have been demonstrated in both infected patients who have seroconverted to anti-HBe and those with fulminant hepatitis B. A donated plasma sample was found to be positive for the hepatitis B surface antigen, but negative for both HBeAg and anti-HBe. The **HBV** DNA titer in the plasma was estimated to be 32 pg/ml, and circulating virus-like particles were observed by electron microscopy. The entire nucleotide sequence of the virus was determined and at least 7 nucleotides were found to be unique when compared with previously reported sequences. These nucleotides created no termination codon in the precore/core, pol, preS/S and HBx open reading frames. The deduced amino acid substitutions were 28 Arg--Gln, 94 His--Tyr, **131** Val--Ile and 132 Phe--Tyr of HBx and 715 Met--Val and 789 Asp--Asn of pol. Furthermore, the precore and core/pregenome promoter contained altered 1764 A, 1766 T and 1768 A. Therefore, **mutations** in regions other than the precore open reading frame can cause defective HBeAg production.

L5 ANSWER 11 OF 16 MEDLINE
ACCESSION NUMBER: 92234447 MEDLINE
DOCUMENT NUMBER: 92234447 PubMed ID: 1568715
TITLE: Genetic alterations in the gene encoding the major **HBsAg**: DNA and immunological analysis of recurrent **HBsAg** derived from monoclonal antibody-treated liver transplant patients.
AUTHOR: McMahon G; Ehrlich P H; Moustafa Z A; McCarthy L A; Dottavio D; Tolpin M D; Nadler P I; Ostberg L
CORPORATE SOURCE: Sandoz Research Institute, East Hanover, New Jersey 07936.
SOURCE: HEPATOLOGY, (1992 May) 15 (5) 757-66.
Journal code: 8302946. ISSN: 0270-9139.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199205
ENTRY DATE: Entered STN: 19920612
Last Updated on STN: 19920612
Entered Medline: 19920526

AB A gene region encoding a segment of the major surface protein, **HBsAg**, of hepatitis B virus was analyzed from serum samples after orthotopic liver transplantation of three hepatitis B virus chronic carrier patients treated with a human anti-hepatitis B virus monoclonal antibody (SDZ OST 577). Each of these three patients became **HBsAg** negative after transplantation and therapy with the human anti-hepatitis B virus monoclonal antibody but returned to **HBsAg** positivity (first detected 143,251 and 252 days after the transplantation). Polymerase chain reaction DNA amplification was performed on DNA from serum samples showing low levels of recurrent **HBsAg** and reduced antigen reactivity with SDZ OST 577 antibody. Polymerase chain reaction DNA included a 230-bp highly conserved, major S gene region that was cloned into M13 bacteriophage; analysis of this DNA segment provided a consensus of DNA sequences for the serum samples exhibiting altered reactivity with the therapeutic monoclonal. Analysis of independent DNA clones from serum samples of patients exhibiting low but detectable recurrent serum levels of posttherapy **HBsAg** revealed the presence of S protein **variant** sequences when compared with polymerase chain reaction DNA derived from the original infected liver or pretherapy serum **HBsAg**. Genetic variation was predominant in a highly conserved peptide domain that has previously been implicated in antibody binding and neutralizing antibody epitopes. In independent patients infected with either adw or ayw hepatitis B virus subtypes, single nucleotide changes resulted in one to two amino acid differences for each **variant allele** (residues 124, 129, **131**, 137, 140 and/or 145) when compared with pretherapy viral DNA. Administration of serum containing one of these **variant** viruses

to a single hepatitis B-naive chimpanzee resulted in subclinical hepatitis and detectable levels of circulating anti-HBs and anti-HBc antibodies 49 and 70 days after virus administration, respectively. Hepatitis B virus DNA was recovered on liver biopsy between 6 and 8 wk after inoculation, although the animal remained persistently seronegative for **HBsAg** . DNA sequence analysis of both primate and patient liver hepatitis B virus confirmed the presence of the DNA encoding the S protein **variant** and associates this DNA with the predominant hepatotropic virus in liver infection.

L5 ANSWER 12 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1999:26871 BIOSIS
DOCUMENT NUMBER: PREV199900026871
TITLE: Hepatocellular proliferation and development of hepatocellular carcinoma: A case-control study in chronic hepatitis C.
AUTHOR(S): Dutta, Usha; Kench, James; Byth, Karen; Khan, Mahbub H.; Lin, Rita; Liddle, Christopher; Farrell, Geoffrey C.
CORPORATE SOURCE: Storr Liver Unit, Dep. Medicine, Westmead Hospital, Westmead NSW 2145 Australia
SOURCE: Human Pathology, (Nov., 1998) Vol. 29, No. 11, pp. 1279-1284.
ISSN: 0046-8177.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Patients with hepatitis C have an increased risk of developing hepatocellular carcinoma (HCC). This is related to the stage of chronic liver disease, as characterized histologically by hepatic fibrosis and architectural distortion, but it is unclear whether histological markers can define the risk of developing HCC. We conducted a case-control immunohistochemical study of Ki-67, a marker for hepatocellular proliferation, in livers of IS patients who had developed HCC more than 2 years after the biopsy specimen had been taken. Using conditional logistic regression analysis, the results were compared with 18 selected controls, who were age-matched patients with hepatitis C of similar histological stage who had not developed HCC. We also examined livers for cellular dysplasia, p53 **mutations**, and bcl-2 overexpression, and assessed whether the results could be correlated with demographic and disease-related variables, such as gender, region of birth, alcohol consumption, severity of liver disease, HCV genotype, and markers of hepatitis B virus (**HBV**) infection. Livers from patients who developed HCC were more often positive for Yi-67 (13 of 18 (72%) v 9 of 18 (50%); P = .06) and tended to have higher mean Yi-67 scores (6 +- 7.5 v 3 +- 4.4; P=.10) compared with control cases. In the HCC-predisposed group, three livers showed large cell dysplasia two were positive for p53 **mutations**, and two for bcl-2 overexpression. In contrast, in the non-HCC group, only one case had dysplasia, and none were positive for immunostaining for p53 or bcl-2 **mutations**. With the exception of one case, all livers with large cell dysplasia or p53 **mutations** and bcl-2 overexpression were also positive for Ki-67. Twelve (55%) of the 22 Ki-67-positive cases were anti-HBc-positive in the serum, in contrast to 2 of 14 (14%) patients in the Ki-67-negative group (P = .0 1). Patients with evidence of past infection with **HBV** were more often Ki-67 positive than those who had no evidence of past infection (85% (11 of **131** v 45% (10 of 22); P = .02). There were no other associations between demographic or disease-related variables and Ki-67 expression. Increased hepatocellular proliferative activity, as assessed by Ki-67 expression, may be one factor indicative of an increased risk of developing HCC among patients with chronic hepatitis C. Furthermore, past infection with **HBV** appears to be an important correlate of increased hepatocelliaar proliferation in hepatitis C.

L5 ANSWER 13 OF 16 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.
ACCESSION NUMBER: 1998:511383 BIOSIS

DOCUMENT NUMBER: PREV199800511383
TITLE: Patterns of circulating hepatitis B surface antigen **variants** among vaccinated children born to hepatitis B surface antigen carrier and non-carrier mothers: A population-based comparative study.
AUTHOR(S): Ho, Mei-Shang (1); Mau, Yi-Chien; Lu, Chih-Feng; Huang, Shiang-Fen; Hsu, Li-Ching; Lin, Sheue-Rong; Hsu, Hsu-Mei
CORPORATE SOURCE: (1) Inst. Biomed. Sci., Acad. Sinica, Taipei 11529, Taiwan China
SOURCE: Journal of Biomedical Science, (Sept.-Oct., 1998) Vol. 5, No. 5, pp. 355-362.
ISSN: 1021-7770.
DOCUMENT TYPE: Article
LANGUAGE: English
AB Hepatitis B virus (**HBV**) **variants** that possessed missense **mutation** within the neutralization epitope of the major S antigen as defined by amino acid residues (aa) 124-147, termed the 'a' determinant **variants**, were identified through a population-based serosurvey of 2,305 children of the vaccinated birth cohorts born after 1986. Data on the 678 nucleotides encoding the S antigen of **HBV** were available for 75 **HBV** strains that were collected from 63 vaccinated children and 12 unvaccinated or incompletely vaccinated children, and 21 **HBV** strains from 25 unvaccinated adults. Among the diverse patterns of one to three amino acid substitutions within the 'a' determinant, 145-Arg occurred most frequently (5/14); other **variants** were: 126-Ala, 127-Thr, 126-Ser/**131**-Asn/133-Thr, 129-His, 129-Arg, 123-Asn/**131**-Ile, 133-Leu, 141-Glu, and 141-Arg/144-Ala. Only one of these **variants** occurred in the 16 hepatitis B surface antigen (**HBsAg**)-carrier children born to **HBsAg**-negative mothers, whereas 12 of these **variants** occurred in the 20 (50%) children born to **HBsAg**-positive mothers. In addition, early administration of **HBV** vaccine within the neonatal period increased the likelihood of the emergence of these **variants** to 64.7% (11/17). Five of the 21 (23.8%) unvaccinated **HBsAg**-carrier adults harbored the 'a' determinant **variants** possessing **mutations** within aa 125-136, i.e., the putative first loop formed by the cysteine disulfide bonds. Vaccinated children were likely to harbor **HBV** **variants** possessing **mutations** involving altered charge of side chains and/or its hydrophobicity of amino acid residues within the putative second loop between aa140 and 146. Our data suggest that emergence of these **HBV** S gene **mutants** in the phase of **HBV** vaccination program would be most common among populations in whom perinatal/vertical transmission of **HBV** is most common, i.e., southeast Asian and the Taiwanese.

L5 ANSWER 14 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1997:86531 CAPLUS
DOCUMENT NUMBER: 126:129061
TITLE: Envelope **variants** of hepatitis B virus in Chinese **HBsAg** negative carriers
AUTHOR(S): Hou, Jinlin; Wang, Zhanhui; Lou, Kangxian; Guo, Yabing; Wang, Yanjun; Liang, Zhisen
CORPORATE SOURCE: Nanfang Hosp., First Military Med. Univ., Guanzhou, 5105115, Peop. Rep. China
SOURCE: Jiefangjun Yixue Zazhi (1996), 21(4), 246-248
CODEN: CFCHBN; ISSN: 0577-7402
PUBLISHER: Jenminjun Chubanshe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese
AB Serol. and virol. studies were performed to identify the envelope **variant** in subjects with or without detectable hepatitis B surface antigen (**HBsAg**). Two types of envelope **variants** of hepatitis B virus (**HBV**) were identified in **HBsAg** neg.

but **HBV** DNA pos. carriers, and compared with **HBsAg** pos. patients with chronic liver diseases. Amino acid substitutions in the immunodominant epitope region of the "A" determinant were detected in 5 cases of carriers, presence of a isoleucine instead of threonine at position **131** was seen in consensus sequences from the Chinese isolated in 3 cases of paid blood donors. A substitution of a methionine to threonine was detected in one patient with chronic liver disease. The study suggests that the envelope **variants** of **HBV** might be responsible for some cases of co-called non A-E hepatitis serol. identified.

L5 ANSWER 15 OF 16 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1995:543645 CAPLUS
DOCUMENT NUMBER: 122:283866
TITLE: Molecular cloning of cDNA for hepatitis B virus protein X and its use for diagnosis
INVENTOR(S): Uchida, Toshikazu; Shikata, Toshio
PATENT ASSIGNEE(S): Mitsubishi Kagaku Kk, Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 7 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 07033797	A2	19950203	JP 1993-180314	19930721

PRIORITY APPLN. INFO.: JP 1993-180314 19930721
AB A cDNA encoding protein X is isolated from the sera of patients infected by hepatitis B virus (**HBV**), but the patients are unable to be diagnosed by conventional methods. The cDNA encodes 134-amino-acid protein X which contains a unique fragment Val-Trp-Arg-Leu (**131** .apprx.134) and residue 73-Leu. The protein X may be a deletion **mutant** of the already known 154-amino-acid protein X. The cDNA may be used for developing diagnostics or vaccines for **HBV**.

L5 ANSWER 16 OF 16 EMBASE COPYRIGHT 2003 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000249318 EMBASE
TITLE: Uneven distribution of **HBV** 16 E6 prototype and **variant** (L83V) oncoprotein in cervical neoplastic lesions.
AUTHOR: Andersson S.; Alemi M.; Rylander E.; Strand A.; Larsson B.; Sallstrom J.; Wilander E.
CORPORATE SOURCE: E. Wilander, Department of Genetics and Pathology, Section of Clinical Cytology, University Hospital, Uppsala, Sweden
SOURCE: British Journal of Cancer, (2000) 83/3 (307-310).
Refs: 27
ISSN: 0007-0920 CODEN: BJCAAI
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
005 General Pathology and Pathological Anatomy
016 Cancer
LANGUAGE: English
SUMMARY LANGUAGE: English
AB A previous Swedish study revealed that both prototype and **variant** HPV16 E6 oncoprotein, occur in about equal numbers in high-grade cervical intraepithelial neoplasia (HCIN), whereas **variant** HPV16 predominates in invasive cervical squamous carcinoma. Most of the malignant HPV16 **variants** contain a common **mutation**, L83V, in the E6 oncoprotein. In the present investigation, 28 HPV16 positive, invasive cervical adenocarcinomas were collected from a total number of **131** adenocarcinomas. These HPV16-positive cases were

evaluated with analysis of the E6 gene, using a recently described PCR-SSCP method for identification of the specific **mutation** (L83V) in the E6 gene. The results obtained were correlated to findings in 103 preinvasive, HCIN, and 31 invasive cervical squamous carcinomas also infected with HPV16. The HPV16 E6 **variant** L83V was present in 40% of the HCIN lesions, in 54% of the invasive adenocarcinomas, in comparison to 81% of the invasive squamous carcinomas. The difference between HCIN and squamous carcinomas was statistically significant, $P < 0.001$, whereas the difference between HCIN and invasive adenocarcinomas was not statistically significant, $P = 0.604$. Prototype HPV16 and its E6 **variant** L83V are both prevalent in preinvasive and invasive cervical lesions in Swedish women. However, the obvious predominance of HPV16 **variant** in squamous carcinomas was not seen in adenocarcinomas. A single amino-acid shift in the HPV16 E6 gene appears to result in a different transforming potential in squamous and glandular cervical lesions.

L Number	Hits	Search Text	DB	Time stamp
1	732	hbv and ("131" or "T131" or "131N" or "T131N")	USPAT; US-PGPUB; DERWENT	2003/06/19 06:26
2	45	hbv same ("131" or "T131" or "131N" or "T131N")	USPAT; US-PGPUB; DERWENT	2003/06/19 06:26